

accompanying application as follows:

Please add the Abstract attached on a separate sheet. ✓

In the Claims

Please cancel Claims 17, 18, 28, 29, 31 and 32 (without prejudice); enter the indicated amendments to Claims 2, 4 to 7, 9 to 16, 19 to 25, 27 and 33; and enter new Claims 34 to 36. ✓ Directions for amendment of claims are indicated on the copy of the attached hand amended ("marked up") original claims, showing in manuscript the amendments that have been made and the origins of the new claims. ✓ Clean forms of new and rewritten claims are included in the attached "Clean Set of Claims" document. ✓

Remarks

This application seeks protection for certain novel compounds that are inhibitors of the serine protease, Factor Xa, and are useful for the treatment of thrombotic disorders. It is the national stage of an international application, the claims of which were drafted in accordance with international practice.

Applicants now wish to amend the application to bring it into conformity with United States patent practice.

For the assistance of the Examiner, a copy of the original claims is attached, as noted above, showing in manuscript the amendments that have been made.

Claims 17, 18, 28, 29, 31 and 32 have been cancelled, without prejudice.

Claims 2, 4 to 6, 9 to 13, 15 to 16, 19 to 24, 27 and 33 have been rewritten in single dependent form.

Claim 2 has been further amended by inserting the value "piperidin-4-yl (which may bear a 1-methyl

10030187 020402

substituent,)" in the definition of  $\text{CHReRf}$  before "or indan-2-yl". Basis for this amendment may be found in the corresponding passage at page 8, lines 22 to 23 of the description.

Claim 7 has been amended by inserting a definition for L, based upon page 11, line 16.

Claim 14 now depends from any one of claims 1 to 13, 15 to 16 and 19 to 22. Claim 25 now depends from claim 14.

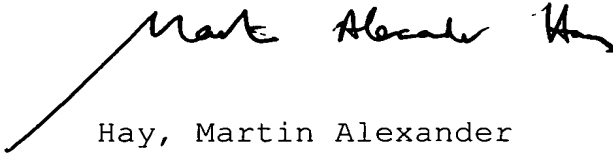
New claim 34 is based upon Claim 26 and is directed to a single compound, 1-(Indole-6-carbonyl-D-phenylglyciny)-4-(1-methylpiperidin-4-yl)piperazine and its physiologically tolerable salts. New Claim 35 is based upon Claim 27, and is directed to a pharmaceutical composition comprising a compound of new Claim 34. Similarly, new Claim 36 is based upon Claim 30, and is directed to a method of combating a thrombotic disorder using a compound of new Claim 34.

For the convenience of the Examiner, it is noted that the compounds of new Claim 34 correspond with formula (I) in Claim 1 in which  $\text{R}_2$  is indol-6-yl, X-X is CONH, Y is CH and has the D-configuration, Cy is phenyl and  $\text{R}_r$  is  $-\text{CHReRf}$  in which  $\text{CHReRf}$  is piperidin-4-yl that bears a methyl group at the 1-position. Currently Claims 1, 2, 7 to 16, 19 to 22, 24 to 27, 30 and 34 to 36 read on these compounds. Claim 33 reads on an intermediate useful in the preparation of these compounds.

Favorable consideration of the application is requested.

10030187-020402

Respectfully submitted,



Hay, Martin Alexander

Agent for Applicants

Registration No. 39,459

Phone: 011 44 1625 500057

Martin A. Hay & Co.,  
13 Queen Victoria Street  
Macclesfield  
Cheshire  
SK11 6LP  
UNITED KINGDOM

February 1, 2002

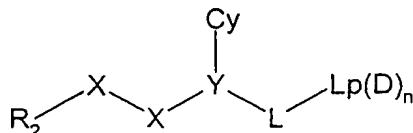
Attachments:    Abstract on separate sheet  
                  Hand-amended (marked-up) Claims  
                  Clean Pending Claims

10030187 020402

- 170 -

Marked Up Version of Claims  
 Claims

1. A serine protease inhibitor compound of formula (I)



5

(I)

wherein:

R<sub>2</sub> is a 5 or 6 membered aromatic carbon ring optionally interrupted by a nitrogen, oxygen or sulphur ring atom, optionally being substituted in the 3 and/or 4 position (in relation to the point of attachment of X-X) by halo, nitro, thiol, haloalkoxy, hydrazido, alkylhydrazido, amino, cyano, haloalkyl, alkylthio, alkenyl, alkynyl, acylamino, tri or difluoromethoxy, carboxy, acyloxy, MeSO<sub>2</sub>- or R<sub>1</sub>, or the substituents at the 3 and 4 positions taken together form a fused ring which is a 5 or 6 membered carbocyclic or heterocyclic ring optionally substituted by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R<sub>1j</sub>, and optionally substituted in the position alpha to the X-X group (i.e. 6 position for a six membered aromatic ring etc) by amino, hydroxy, halo, alkyl, carboxy, alkoxy, carbonyl, cyano, amido, aminoalkyl, alkoxy or alkylthio with the proviso that R<sub>2</sub> cannot be aminoisoquinolyl;

each X independently is a C, N, O or S atom or a CO,

CR<sub>1a</sub>, C(R<sub>1a</sub>)<sub>2</sub> or NR<sub>1a</sub> group, at least one X being C, CO, CR<sub>1a</sub> or C(R<sub>1a</sub>)<sub>2</sub>;

each R<sub>1a</sub> independently represents hydrogen or hydroxyl, alkoxy, alkyl, aminoalkyl, hydroxyalkyl alkoxyalkyl, alkoxy, carbonyl, alkylaminocarbonyl, alkoxy, carbonyl, amino,

acyloxymethoxycarbonyl or alkylamino optionally substituted by hydroxy, alkylamino, alkoxy, oxo, aryl or cycloalkyl;

R<sub>1</sub> is as defined for R<sub>1a</sub>, provided that R<sub>1</sub> is not

unsubstituted aminoalkyl;

Y (the  $\alpha$ -atom) is a nitrogen atom or a  $CR_{1b}$  group;

Cy is a saturated or unsaturated, mono or poly cyclic, homo or heterocyclic group, optionally substituted by groups

5  $R_{3a}$  or  $R_{3i}X_i$ ;

each  $R_{3a}$  independently is  $R_{1c}$ , amino, halo, cyano, nitro, thiol, alkylthio, alkylsulphonyl, alkylsulphenyl, triazolyl, imidazolyl, tetrazolyl, hydrazido, alkylimidazolyl, thiazolyl, alkylthiazolyl, alkyloxazolyl, oxazolyl, alkylsulphonamido,

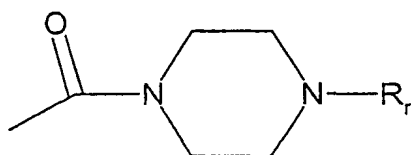
10 alkylaminosulphonyl, aminosulphonyl, haloalkoxy, haloalkyl, a group of the formula  $-C(X^3)N(R^{11})R^{12}$  (wherein  $X^3$  is O or S; and  $R^{11}$  and  $R^{12}$  are independently selected from hydrogen, methyl or ethyl or together with the nitrogen atom to which they are attached form a pyrrolidin-1-yl, piperidin-1-yl or morpholino group), or  $-OCH_2O-$  which is bonded to two adjacent ring atoms in Cy;

$X_i$  is a bond, O, NH or  $CH_2$ ;

$R_{3i}$  is phenyl, pyridyl or pyrimidinyl optionally substituted by  $R_{3a}$ ;

20  $R_{1b}$ ,  $R_{1c}$  and  $R_{1j}$  are as defined for  $R_{1a}$ ; and

$-L-Lp(D)_n$  is of the formula:



in which  $R_r$  is  $-(CH_2)_c-R_c$ ,  $-CHR_eR_f$ ,  $-CH_2-CHR_eR_f$ ,

$-CH_2-CH_2-CHR_eR_f$ , or  $R_g$  in which c is 1 or 2;  $R_c$  is thienyl,

25 thiazolyl (which may bear an amino substituent), isothiazolyl, oxazolyl, isoxazolyl, pyrazolyl, imidazolyl, pyridyl (which may bear an alkylsulphonyl, aminosulphonyl,

alkylaminosulphonyl, alkylaminocarbonyl, amino, amido, (1-4C)alkoxycarbonyl, carboxy, acetyl amino, chloro, fluoro,

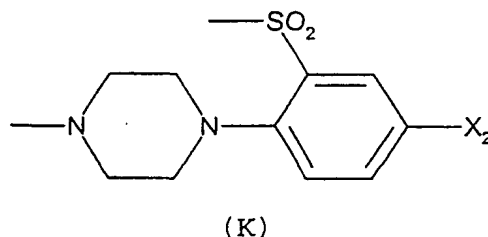
30 cyano, (1-3C)alkyl, trifluoromethyl, methoxy, ethoxy, nitro, hydroxy, alkylsulphonylamino, triazolyl or tetrazolyl

10030187-020402

substituent), pyrimidinyl, pyridazinyl, pyrazinyl or phenyl (which may bear a methyl, methylamino, dimethylamino, carboxy, dialkylaminosulphonyl, alkylsulphonyl, aminosulphonyl, alkylaminosulphonyl, alkylaminocarbonyl, amino, amido, 5 alkoxy, acetyl, chloro, fluoro, cyano, methoxy, ethoxy, nitro, hydroxy, alkylsulphonylamino, triazolyl or tetrazolyl substituent); each of  $R_e$  and  $R_f$  independently is hydrogen or  $C_{1-3}$ alkyl; or  $CH(R_e)R_f$  is cyclopentyl (which may bear a hydroxy, amino, (1-3C)alkoxy, (1-3C)hydroxyalkyl, (1-10 3C)alkyl, carboxy, methoxycarbonyl or ethoxycarbonyl substituent at the 3- or 4-position), cyclohexyl (which may bear a hydroxy, amino, (1-3C)alkoxy, (1-3C)hydroxyalkyl, (1-3C)alkyl, carboxy, methoxycarbonyl or ethoxycarbonyl substituent at the 3- or 4-position), tetrahydropyran-4-yl, 15 tetrahydrothiopyran-4-yl, pyrrolidin-3-yl (which may bear a hydroxy, amino, (1-3C)alkoxy, (1-3C)hydroxyalkyl, (1-3C)alkyl, carboxy, methoxycarbonyl or ethoxycarbonyl substituent at the 1-position), piperidin-4-yl (which may bear a hydroxy, amino, (1-3C)alkoxy, (1-3C)hydroxyalkyl, (1-3C)alkyl, carboxy, 20 methoxycarbonyl or ethoxycarbonyl substituent at the 1-position), or indan-2-yl; and  $R_g$  is 2-methylsulphonylphenyl which may bear a 4-fluoro substituent or  $R_g$  is  $\lambda^6$ -1,1-dioxobenzo[b]thiophen-7-yl;

or a physiologically-tolerable salt thereof;

25 provided that  $Lp(D)_n$  is not of the formula (K):



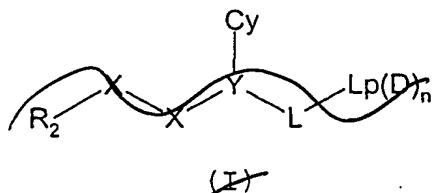
wherein  $X_2$  is fluoro or hydrogen.

30 compound according to claim 1

2. A ~~serine protease inhibitor compound of formula (I)~~

(amended)

- 173 -



wherein,

~~R<sub>2</sub> is a 5 or 6 membered aromatic carbon ring optionally~~  
 5 interrupted by a nitrogen, oxygen or sulphur ring atom,  
 optionally being substituted in the 3 and/or 4 position (in  
 relation to the point of attachment of X-X) by halo, nitro,  
 thiol, haloalkoxy, hydrazido, alkylhydrazido, amino, cyano,  
 haloalkyl, alkylthio, alkenyl, alkynyl, acylamino, tri or  
 10 difluoromethoxy, carboxy, acyloxy, MeSO<sub>2</sub>- or R<sub>1</sub>, or the  
 substituents at the 3 and 4 positions taken together form a  
 fused ring which is a 5 or 6 membered carbocyclic or  
 heterocyclic ring optionally substituted by halo, haloalkoxy,  
 haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl,  
 15 alkynyl or R<sub>1j</sub>, and optionally substituted in the position  
 alpha to the X-X group (i.e. 6 position for a six membered  
 aromatic ring etc) by amino, hydroxy, halo, alkyl, carboxy,  
 alkoxycarbonyl, cyano, amido, aminoalkyl, alkoxy or alkylthio  
 with the proviso that R<sub>2</sub> cannot be aminoisoquinolyl;

20 each X independently is a C, N, O or S atom or a CO,  
 CR<sub>1a</sub>, C(R<sub>1a</sub>)<sub>2</sub> or NR<sub>1a</sub> group, at least one X being C, CO, CR<sub>1a</sub>  
 or C(R<sub>1a</sub>)<sub>2</sub>;

each R<sub>1a</sub> independently represents hydrogen or hydroxyl,  
 alkoxy, alkyl, aminoalkyl, hydroxyalkyl alkoxyalkyl,  
 25 alkoxycarbonyl, alkylaminocarbonyl, alkoxycarbonylamino,  
 acyloxymethoxycarbonyl or alkylamino optionally substituted by  
 hydroxy, alkylamino, alkoxy, oxo, aryl or cycloalkyl;

R<sub>1</sub> is as defined for R<sub>1a</sub>, provided that R<sub>1</sub> is not  
 unsubstituted aminoalkyl;

30 ~~Y (the α atom) is a nitrogen atom or a CR<sub>1b</sub> group;~~

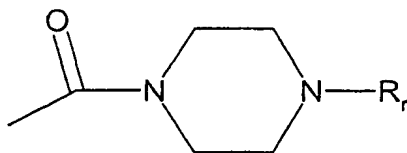
Cy is a saturated or unsaturated, mono or poly cyclic,  
 homo or heterocyclic group, optionally substituted by groups

R<sub>3a</sub> or phenyl optionally substituted by R<sub>3a</sub>;

each R<sub>3a</sub> independently is R<sub>1c</sub>, amino, halo, cyano, nitro, thiol, alkylthio, alkylsulphonyl, alkylsulphenyl, triazolyl, imidazolyl, tetrazolyl, hydrazido, alkyl imidazolyl, thiazolyl, alkyl thiazolyl, alkyl oxazolyl, oxazolyl, alkylsulphonamido, alkylaminosulphonyl, aminosulphonyl, haloalkoxy and haloalkyl;

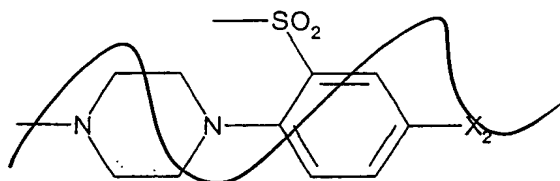
~~R<sub>1b</sub>, R<sub>1c</sub> and R<sub>1j</sub> are as defined for R<sub>1a</sub> and~~

-L-Lp(D)<sub>n</sub> is of the formula:



in which R<sub>r</sub> is -(CH<sub>2</sub>)<sub>c</sub>-R<sub>c</sub>, -CHR<sub>e</sub>R<sub>f</sub>, -CH<sub>2</sub>-CHR<sub>e</sub>R<sub>f</sub>, or R<sub>g</sub> in which c is 1 or 2; R<sub>c</sub> is pyridyl or phenyl (which phenyl may bear a fluoro, chloro, methyl, CONH<sub>2</sub>, SO<sub>2</sub>NH<sub>2</sub>, methylaminosulphonyl, dimethylaminosulphonyl, methoxy or methylsulphonyl substituent); each of R<sub>e</sub> and R<sub>f</sub> independently is hydrogen or C<sub>1-3</sub>alkyl; or CHR<sub>e</sub>R<sub>f</sub> is cyclopentyl (which may bear a methyl, ethyl or hydroxymethyl substituent at the 3- or 4-position), cyclohexyl (which may bear a methyl, ethyl or hydroxymethyl, (1-3C)alkyl, carboxy, methoxycarbonyl or ethoxycarbonyl substituent at the 3- or 4-position), tetrahydropyran-4-yl, tetrahydrothiopyran-4-yl, pyrrolidin-3-yl (which may bear a 1-methyl substituent), <sup>piperidin-4-yl (which may bear a 1-methyl substituent)</sup> or indan-2-yl; and R<sub>g</sub> is 2-methylsulphonylphenyl which may bear a 4-fluoro substituent or R<sub>g</sub> is λ<sup>6</sup>-1,1-dioxobenzo[b]thiophen-7-yl.

~~or a physiologically tolerable salt thereof, provided that Lp(D)<sub>n</sub> is not of the formula (K):~~



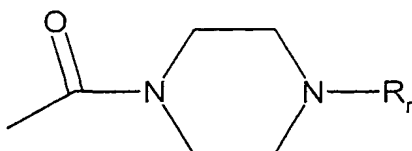


- 175 -

(K)

~~wherein  $X_2$  is fluoro or hydrogen.~~

- 5 3. A compound according to claim 1 wherein  $-L-Lp(D)_n$  is of the formula:



in which  $R_f$  is  $-(CH_2)_c-R_c$ ; in which  $c$  is 2;  $R_c$  is thienyl, thiazolyl (which may bear an amino substituent),  
 10 isothiazolyl, oxazolyl, isoxazolyl, pyrazolyl, imidazolyl, pyridyl (which may bear an amino, methoxycarbonyl, carboxy, fluoro, cyano, methyl, methylsulphonyl, aminosulphonyl, methylaminosulfonyl, dimethylaminosulfonyl, or trifluoromethyl  
 15 substituent), pyrimidinyl, pyridazinyl, pyrazinyl or phenyl (which phenyl may bear a fluoro, chloro, cyano, methyl, amino, methylsulphonyl, aminosulphonyl, methylaminosulphonyl, dimethylaminosulphonyl, methylamino, dimethylamino, carboxy, methoxycarbonyl or methoxy substituent).

(amended)

- 20 4. A compound according to ~~any one of claims 1 to 3~~ wherein  $R_c$  is thiazolyl (which may bear an amino substituent), pyrimidinyl, pyrazolyl, imidazolyl, pyridyl (which may bear a methylsulphonyl, aminosulphonyl, methylaminosulfonyl, dimethylaminosulfonyl, fluoro, cyano, methyl or  
 25 trifluoromethyl substituent), pyridazinyl, pyrazinyl or phenyl (which phenyl may bear a fluoro, chloro, cyano, methyl, amino, methylamino, dimethylamino, carboxy, methoxycarbonyl, methylsulphonyl, aminosulphonyl, methylaminosulfonyl, dimethylaminosulfonyl, or methoxy substituent).

(amended)

- 30 5. A compound according to ~~any one of claims 1 to 4~~ wherein

Rc is thiazolyl (which may bear an amino substituent), pyrazolyl, imidazolyl, pyridyl (which may bear a fluoro, cyano, methyl or trifluoromethyl substituent), pyridazinyl or pyrazinyl.

5

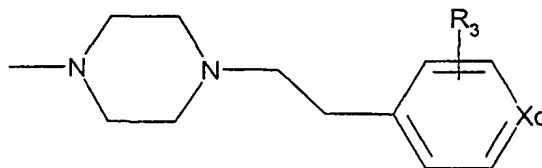
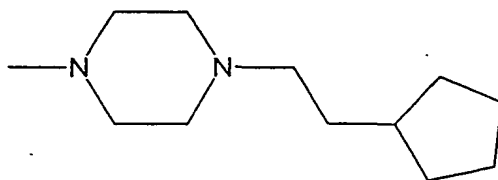
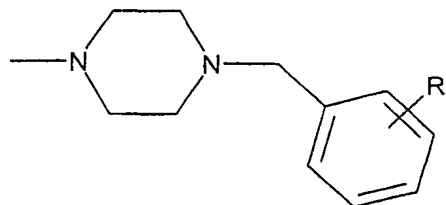
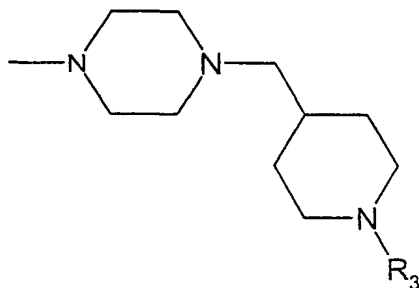
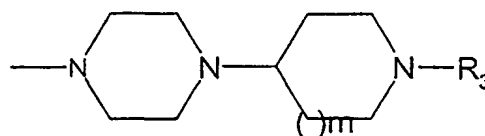
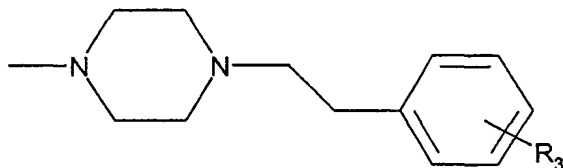
(amended)

6. A compound according to ~~any one of claims 1 to 5~~ wherein Rc is thiazol-2-yl, 2-aminothiazol-4-yl, pyrazol-1-yl, pyrazol-4-yl, pyridazin-3-yl, imidazol-1-yl, imidazol-4-yl, pyrazin-2-yl, pyrid-2-yl, pyrid-3-yl, pyrid-4-yl, 3-fluoropyrid-4-yl, 2-cyanopyrid-4-yl, 2-methylpyrid-4-yl or 2-trifluoromethylpyrid-6-yl.

(amended)

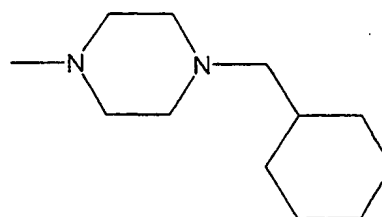
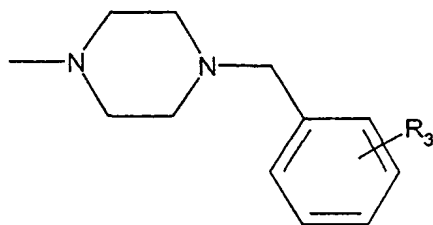
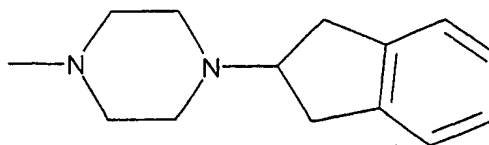
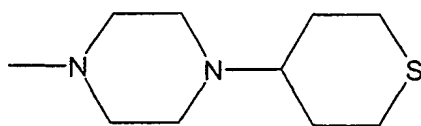
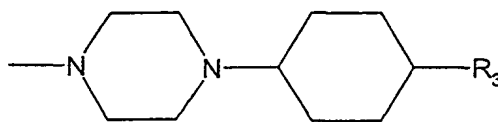
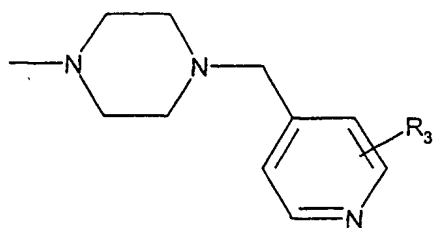
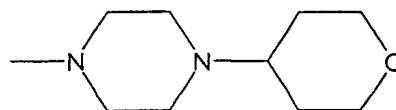
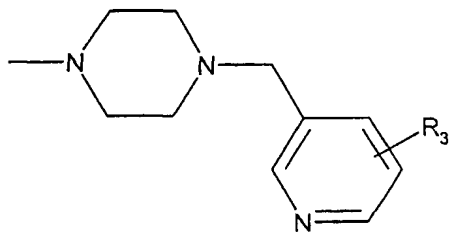
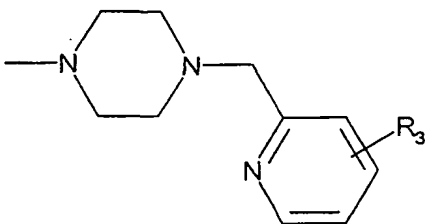
L is CO and

7. A compound according to claim 1 wherein -Lp(D)n is of the formula:



10030187-020402

- 177 -

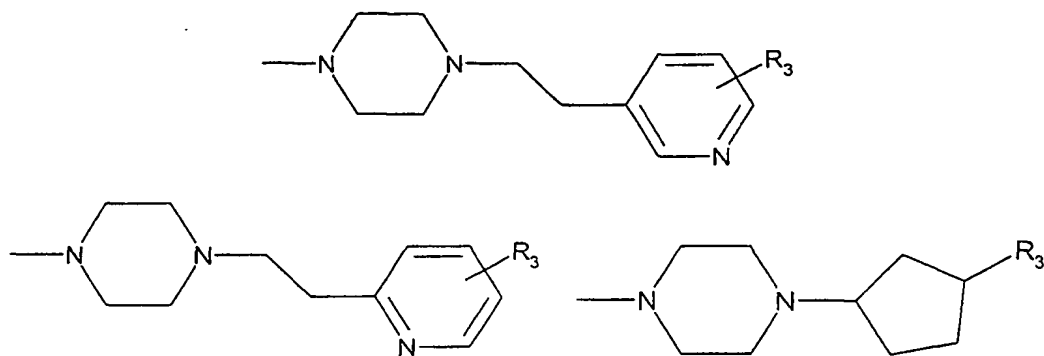


10030187.020402

5

10

- 178 -



wherein;

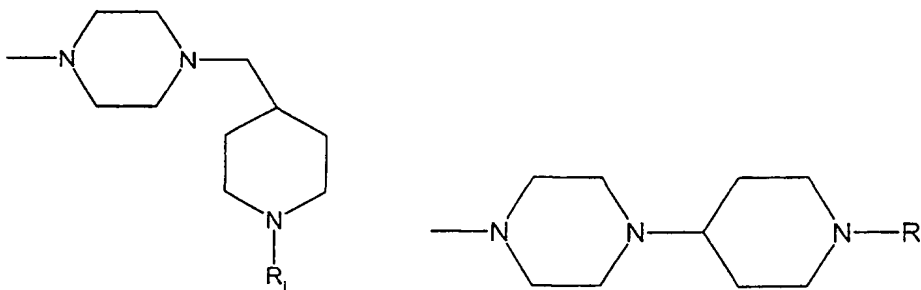
m represents 0 or 1;

5  $X^0$  represents CH or N; and

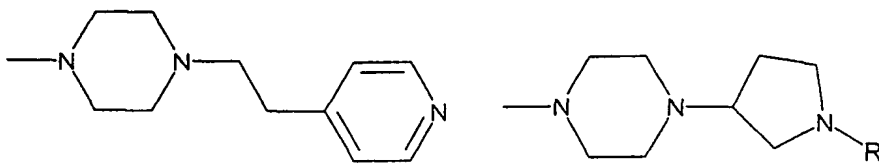
when  $R_3$  is present as a substituent on an aromatic ring,  
it is selected from hydrogen, alkylsulphonyl, aminosulphonyl,  
alkylaminosulphonyl, alkylaminocarbonyl, amino, amido,  
alkoxycarbonyl, acetyl amino, chloro, fluoro, cyano, methoxy,  
10 ethoxy, nitro, hydroxy, alkylsulphonylamino, triazolyl and  
tetrazolyl; and

when  $R_3$  is present as a substituent on a saturated ring,  
it is selected from hydrogen, hydroxy, amino, (1-3C)alkoxy,  
(1-3C)hydroxyalkyl, (1-3C)alkyl, carboxy, methoxycarbonyl and  
15 ethoxycarbonyl.

8. A compound according to claim 7 wherein  $-Lp(D)_n$  is of the  
formula:



- 179 -



wherein  $R_1$  is hydrogen or (1-6C)alkyl.

(amended)

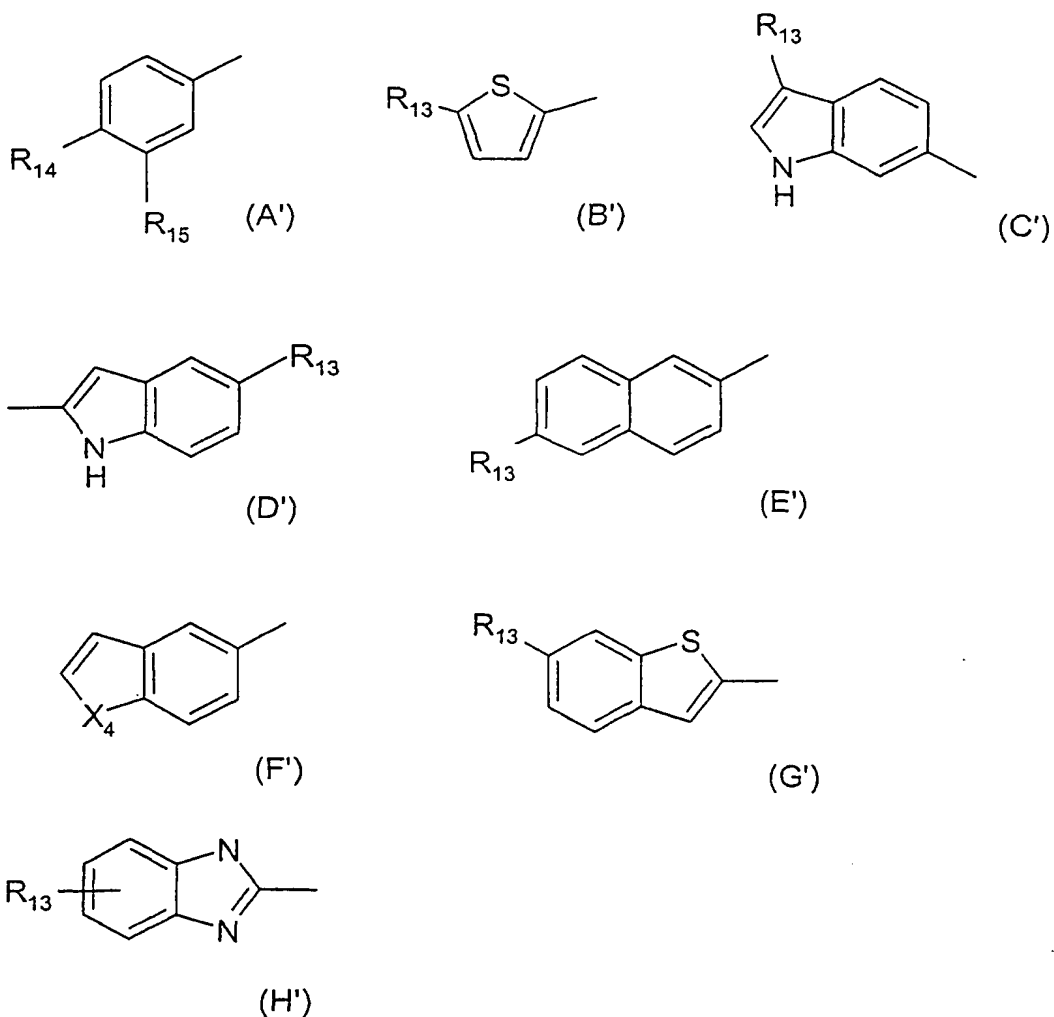
9. A compound according to ~~any one of claims 1 to 8~~ wherein  $R_2$  is phenyl, thien-2-yl, naphthyl, indol-2-yl, indol-6-yl, benzo[b]furan-5-yl, benzo[b]thiophen-2-yl or benzimidazol-2-yl (each of which is optionally substituted as defined in claim 1).

(amended)

10. A compound according to ~~any one of claims 1 to 9~~ wherein optional substituents for  $R_2$  are selected from: fluoro, chloro, bromo, iodo, nitro, thiol, difluoromethoxy, trifluoromethoxy, hydrazido, methylhydrazido, amino, cyano, trifluoromethyl, methylthio, vinyl, ethynyl, acetylamino, carboxy, acetoxy, hydroxy, methyl, ethyl, amido ( $\text{CONH}_2$ ), aminomethyl, methoxy and ethoxy.

(amended)

11. A compound according to ~~any one of claims 1 to 10~~ wherein  $R_2$  is selected from one of the formula (A') to (H'):



wherein  $X_4$  is O or S,  $R_{13}$  is selected from hydrogen, fluoro, [except for (C')] chloro or methyl and  $R_{14}$  is selected from hydrogen, methyl, ethyl, fluoro, chloro, and methoxy and  
 5  $R_{15}$  is selected from hydrogen, methyl, fluoro, chloro and amino.

(amended)

12. A compound according to claims ~~1 to 11~~, wherein  $R_2$  is 4-chlorophenyl, 4-methoxyphenyl, 3-amino-4-chlorophenyl, indol-  
 10 2-yl, 5-chloroindol-2-yl, indol-6-yl, 3-chloroindol-6-yl or 3-methylindol-6-yl.

(amended)

13. A compound according to ~~any one of claims 1 to 12~~ wherein

-X-X- is -CONH-.

(amended)

, 15 to 16 and 19 to 22

14. A compound according to any one of claims 1 to 13 wherein Y is CH.

5

(amended)

15. A compound according to ~~any one of claims 1 to 14~~ wherein Cy is an optionally R<sub>3a</sub> substituted: phenyl, pyridyl, thienyl, thiazolyl, naphthyl, piperidinyl, furanyl, pyrrolyl, isoxazolyl, isothiazolyl, pyrazolyl, oxazolyl, imidazolyl,

10 1,2,4-thiadiazolyl, 1,3,4-thiadiazolyl, pyrimidinyl, pyridazinyl, quinolyl, isoquinolyl, benzofuryl, benzothienyl or cycloalkyl group, or a phenyl group substituted by R<sub>3i</sub>X<sub>i</sub> in which X<sub>i</sub> is a bond, O, NH or CH<sub>2</sub> and R<sub>3i</sub> is phenyl, pyridyl or pyrimidyl optionally substituted by R<sub>3a</sub>.

15

(amended)

16. A compound according to ~~any one of claims 1 to 14~~ wherein Cy is an optionally R<sub>3a</sub> substituted: phenyl, pyridyl, thienyl, thiazolyl, naphthyl, piperidinyl or cycloalkyl group.

(cancelled on national phase entry)

20 17. ~~A compound according to any one of claims 1 to 16 wherein R<sub>3a</sub> is selected from hydrogen, hydroxyl, alkoxy, alkyl (optionally substituted by hydroxy, alkylamino, alkoxy, oxo, aryl or cycloalkyl), aminoalkyl (optionally substituted by hydroxy, alkylamino, alkoxy, oxo, aryl or cycloalkyl), hydroxyalkyl (optionally substituted by hydroxy, alkylamino, alkoxy, oxo, aryl or cycloalkyl), alkoxyalkyl, alkoxycarbonyl, alkylaminocarbonyl, alkoxycarbonylamino, alkylamino (optionally substituted by hydroxy, alkylamino, alkoxy, oxo, aryl or cycloalkyl), amino, halo, cyano, nitro, thiol, alkylthio, alkylsulphonyl, alkylsulphenyl, alkylsulphonamido, alkylaminosulphonyl, aminosulphonyl, haloalkoxy, haloalkyl, a group of the formula -C(X<sup>3</sup>)N(R<sup>11</sup>)R<sup>12</sup> (wherein X<sup>3</sup> is O or S; and R<sup>11</sup> and R<sup>12</sup> are independently selected from hydrogen, methyl or ethyl or together with the nitrogen atom to which~~

10030187 020402

~~they are attached form a pyrrolidin-1-yl, piperidin-1-yl or morpholino group) and -OCH<sub>2</sub>O- which is bonded to two adjacent ring atoms in Cy~~

~~(cancelled on national phase entry)~~

- 5 18. ~~A compound according to any one of claims 1 to 16 wherein~~  
~~R<sub>3a</sub> is selected from hydrogen, hydroxyl, alkoxy, alkyl~~  
~~(optionally substituted by hydroxy, alkylamino, alkoxy, oxo,~~  
~~aryl or cycloalkyl), hydroxyalkyl (optionally substituted by~~  
~~hydroxy, alkylamino, alkoxy, oxo, aryl or cycloalkyl),~~  
10 ~~alkoxyalkyl, alkoxycarbonyl, alkylaminocarbonyl,~~  
~~alkoxycarbonylamino, alkylamino (optionally substituted by~~  
~~hydroxy, alkylamino, alkoxy, oxo, aryl or cycloalkyl),~~  
~~aminoalkyl (substituted by hydroxy, alkylamino, alkoxy, oxo,~~  
~~aryl or cycloalkyl), amino, halo, cyano, nitro, thiol,~~  
15 ~~alkylthio, alkylsulphonyl, alkylsulphenyl, alkylsulphonamido,~~  
~~alkylaminosulphonyl, aminosulphenyl, haloalkoxy and haloalkyl~~

~~(amended)~~

15

19. ~~A compound according to any one of claims 1 to 16 wherein~~  
~~R<sub>3a</sub> is selected from hydrogen, hydroxyl, methoxy, ethoxy,~~  
20 ~~methyl, ethyl, methylaminomethyl, dimethylaminomethyl,~~  
~~hydroxymethyl, carboxy, methoxymethyl, methoxycarbonyl,~~  
~~ethoxycarbonyl, methylaminocarbonyl, dimethylamino-carbonyl,~~  
~~aminomethyl, CONH<sub>2</sub>, CH<sub>2</sub>CONH<sub>2</sub>, acetylamino,~~  
~~methoxycarbonylamino, ethoxycarbonylamino, t-~~  
25 ~~butoxycarbonylamino, amino, fluoro, chloro, bromo, cyano,~~  
~~nitro, thiol, methylthio, methylsulphonyl, ethylsulphonyl,~~  
~~methylsulphenyl, methylsulphonylamido, ethylsulphonylamido,~~  
~~methylaminosulphonyl, ethylaminosulphonyl, aminosulphonyl,~~  
~~trifluoromethoxy, trifluoromethyl, bromo, -OCH<sub>2</sub>O- (which is~~  
30 ~~bonded to two adjacent ring atoms in Cy) and -C(X<sup>3</sup>)N(R<sup>11</sup>)R<sup>12</sup>~~  
~~(wherein X<sup>3</sup> is O or S and R<sup>11</sup> and R<sup>12</sup> are independently~~  
~~selected from hydrogen, methyl or ethyl or together with the~~  
~~nitrogen atom to which they are attached form a pyrrolidin-1-~~  
~~yl, piperidin-1-yl or morpholino group).~~

10030187 020402

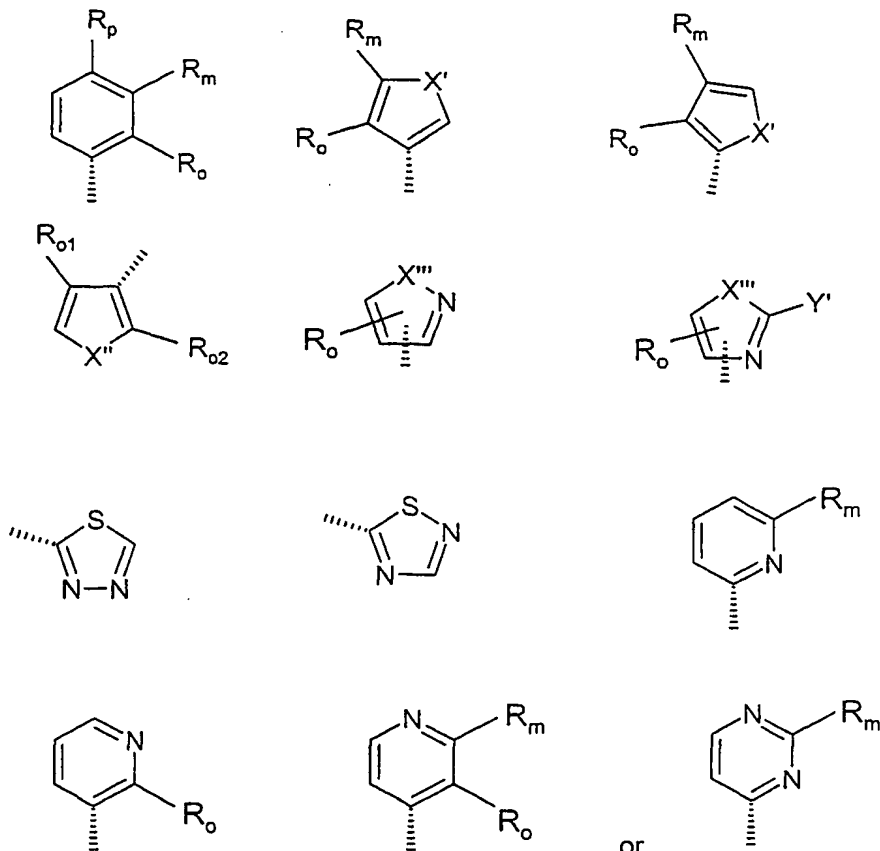


*(amended)*

20. / A compound according to ~~any one of claims 1 to 16~~ wherein  
R<sub>3a</sub> is selected from hydrogen, hydroxyl, methoxy, ethoxy,  
methyl, ethyl, methylaminomethyl, dimethylaminomethyl,  
5 hydroxymethyl, carboxy, methoxymethyl, methoxycarbonyl,  
ethoxycarbonyl, methylaminocarbonyl, dimethylamino-carbonyl,  
aminomethyl, CONH<sub>2</sub>, CH<sub>2</sub>CONH<sub>2</sub>, acetylamino,  
methoxycarbonylamino, ethoxycarbonylamino, t-  
butoxycarbonylamino, amino, fluoro, chloro, cyano, nitro,  
10 thiol, methylthio, methylsulphonyl, ethylsulphonyl,  
methylsulphenyl, methylsulphonylamido, ethylsulphonylamido,  
methylaminosulphonyl, ethylaminosulphonyl, aminosulphonyl,  
trifluoromethoxy and trifluoromethyl.

*(amended)*

- 15 21. / A compound according to ~~any one of claims 1 to 14~~ wherein  
Cy is selected from:



wherein:

$X'$  is selected from O, S and NMe;

$X''$  is selected from O and S;

$X'''$  is selected from O, S, NH and NMe;

$Y'$  is selected from hydrogen, amino and methyl;

$R_o$  is selected from hydrogen, methyl, fluoro, chloro, trifluoromethyl, methoxy, methylthio, methylsulphinyl and methylsulphonyl;

$R_m$  is selected from hydrogen, methyl, fluoro, chloro, trifluoromethyl, methoxy, methylthio, methylsulphinyl, methylsulphonyl, carboxy, methoxycarbonyl and a group of the formula  $-C(X^3)N(R^{11})R^{12}$  (wherein  $X^3$  is O or S and  $R^{11}$  and  $R^{12}$  are independently selected from hydrogen, methyl or ethyl or together with the nitrogen atom to which they are attached form a pyrrolidin-1-yl, piperidin-1-yl or morpholino group);  $R_p$  is selected from hydrogen and fluoro; or

$R_O$  and  $R_m$  or  $R_m$  and  $R_p$  form an  $-OCH_2O-$  group; or  
 $R_O$  and  $R_m$  together with the ring to which they are attached  
 form a 5 or 6 membered aryl or heteroaryl ring (wherein the  
 heteroaryl ring contains 1 or 2 heteroatoms selected from  
 5 nitrogen, oxygen and sulfur);

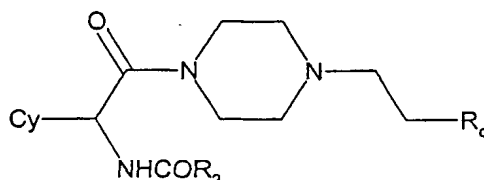
one of  $R_{O1}$  and  $R_{O2}$  is hydrogen and the other is  $R_O$ ;

(amended)

22. A compound according to ~~any one of claims 1 to 14~~ wherein  
 Cy is selected from phenyl, 2-chlorophenyl, 2-methoxyphenyl,  
 10 4-carbamoylphenyl, pyrid-2-yl, pyrid-4-yl, thien-2-yl, thien-  
 3-yl, furan-2-yl, furan-3-yl, imidazol-2-yl, thiazol-2-yl,  
 thiazol-4-yl, thiazol-5-yl and quinolin-4-yl.

(amended)

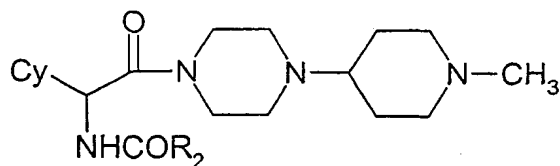
23. A compound of the formula:



or a physiologically-tolerable salt thereof, wherein Cy,  $R_2$   
 and  $R_6$  are as defined in ~~any one of claims 1 to 22~~.

(amended)

24. A compound of the formula:



or a physiologically-tolerable salt thereof, wherein Cy and  $R_2$   
 are as defined in ~~any one of claims 1 to 24~~.

(amended)

14

25. A compound as claimed in ~~any one of Claims 1 to 24~~, in  
 which the alpha atom in Y is carbon and has the conformation  
 that would result from construction from a D- $\alpha$ -aminoacid  
 $NH_2-CR_{1b}(Cy)-COOH$  where the  $NH_2$  represents part of X-X.

10030187.020402

26. A compound as claimed in Claim 1, which is selected from:  
1-(Indole-6-carbonyl-D-phenylglyciny1)-4-[2-(4-pyridiny1)-  
ethyl]piperazine;

5 1-(3-Chloroindole-6-carbonyl-D-phenylglyciny1)-  
4-[2-(4-pyridiny1)ethyl]piperazine;

1-(4-Methoxybenzoyl-D-phenylglyciny1)-4-(1-methylpiperidin-4-  
yl)piperazine;

10 1-(Indole-6-carbonyl-D-phenylglyciny1)-4-(1-methylpiperidin-4-  
yl)piperazine;

1-(4-Methoxybenzoyl-D-(2-chlorophenyl)glyciny1)-4-(1-methyl-  
piperidin-4-yl)piperazine;

1-(Indole-6-carbonyl-D-(2-chlorophenyl)glyciny1)-4-(1-methyl-  
piperidin-4-yl)piperazine; and

15 1-(4-Methoxybenzoyl-D-(2-trifluoromethylphenyl)glyciny1)-4-(1-  
methylpiperidin-4-yl)piperazine;

and physiologically-tolerable salts thereof.

*(amended)*

20 27. A pharmaceutical composition, which comprises a compound  
as claimed in ~~any one of~~ Claims 1 ~~to 26~~ together with at least  
one pharmaceutically acceptable carrier or excipient.

*(cancelled on national phase entry)*

28. ~~A compound as claimed in any one of Claims 1 to 26, for  
use in therapy.~~

25 *(cancelled on national phase entry)*

29. ~~Use of a compound as claimed in any one of Claims 1 to 26  
for the manufacture of a medicament for the treatment of a  
thrombotic disorder.~~

30 30. A method of treatment of a human or non-human animal body  
to combat a thrombotic disorder, which comprises administering  
to said body an effective amount of a compound as claimed in  
claim 1.

10030187.020402

(cancelled on national phase entry)

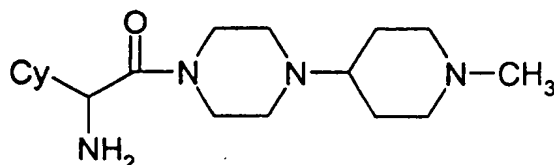
31. ~~A pharmaceutical composition comprising a compound as claimed in any one of claims 1 to 26 for use to combat a thrombotic disorder.~~

(cancelled on national phase entry)

5 32. ~~A compound of formula I as claimed in claim 1 and named in any of the Examples herein, or a physiologically tolerable salt thereof.~~

(amended)

10 33. A compound of the formula



or a salt thereof.

in which Cy is as defined in claim 1,

10030187.020402